Amendment to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1-6 (Canceled)

- 7. (Withdrawn) A method to determine whether a high plasma cholesterol level in a host is due to a genetic alteration of the host's apoB-100 protein comprising administering a LDL clearance enhancing drug to the patient, observing a lower than normal decrease in plasma cholesterol level, and then isolating and evaluating the host's apoB-100 protein.
- 8. (Withdrawn) A method to determine whether a high plasma cholesterol level in a host is due to a genetic alteration of the host's apoB-100 protein comprising exposing the host's apoB-100 protein to an LDL clearance enhancing drug in vitro under conditions in which the host's apoB-100 protein and the drug can form a complex, and then isolating and evaluating the change in conformation of the host 's apoB-100 protein caused by any complexation.
- 9. (Currently Amended) A method to determine if a compound causes a change in the structure of apolipoprotein B-100 in a cholesterol-containing low density lipoprotein thus increasing the binding of an epitope on the apolipoprotein B-100 to the LDL-receptor, comprising:
- (i) mixing the compound with and allowing it to bind to cholesterol-containing low density lipoprotein forming a complex;
- (ii) exposing the complex to a first capture antibody that is attached to a solid phase material and is directed to the epitope on apolipoprotein B-100 that binds to the LDL-receptor, forming a combination;
 - (iii) using a second antibody which binds to the combination;
- (iv) detecting the second antibody bound to the combination by the addition of a third antibody to which is attached a label and binds the second antibody;

U.S.S.N. 09/436,892 Amendment dated October 22, 2004 Reply to Office Action dated June 22, 2004

(v) quantifying the amount of the captured complex by quantifying the amount of label; and

(vi) comparing the amount of cholesterol-containing low density lipoprotein captured by the assay to a control, wherein an increase in the amount of cholesterol-containing low density lipoprotein captured indicates an increased binding to the low density lipoprotein receptor.

10. (canceled)

- 11. (Withdrawn) A method for lowering plasma cholesterol in a host comprising administering an effective amount of a compound that binds to cholesterol-carrying lipoprotein in a manner that alters the three dimensional configuration of the lipoprotein and increases the binding affinity of the apoB-100 protein to the LDL receptor; wherein the LDL-clearance enhancing drug is not probucol or a mono- or di-ester of probucol, not a compound described in WO 98/09773, and not a silyl compound described in U.S. Patent Nos. 5,155,250 or 5,608,095.
- 12. (Withdrawn) The method of claim 11, wherein the LDL receptor is on the surface of hepatic cells.
- 13. (Withdrawn) The method of claim 11, wherein the cholesterol-carrying liproprotein is LDL.
- 14. (Withdrawn) The method of claim 11, wherein the cholesterol-carrying liproprotein is VLDL.
- 15. (Previously presented) A method for assessing whether a compound first binds to a cholesterol-containing lipoprotein, enhancing the binding of the cholesterol-containing lipoprotein to a low density lipoprotein hepatic receptor and thus lowering plasma cholesterol, the method comprising:

3

- (a) allowing the compound to form a complex with a cholesterol-containing lipoprotein in vivo,
 - (b) isolating the resulting complex, and
- (c) determining whether the formation of the complex causes a change in the three dimensional conformation of apoB-100 in the cholesterol-containing lipoprotein that enhances the binding of the lipoprotein to the LDL hepatic receptor.
- 16. (Withdrawn) A method for lowering plasma cholesterol in a host comprising administering an effective amount of a compound that binds to cholesterol-carrying lipoprotein in a manner that alters the three dimensional configuration of the lipoprotein and increases the binding affinity of the apoB-100 protein to the LDL receptor in combination or alternation with a second drug that lowers cholesterol via a different biological pathway; wherein the LDL-clearance enhancing drug is not probucol or a mono- or di-ester of probucol, not a compound described in WO 98/09773, and not a silyl compound described in U.S. Patent Nos. 5,155,250 or 5,608,095.
- 17. (Withdrawn) The method of claim 16, wherein the LDL receptor is on the surface of hepatic cells.
- 18. (Withdrawn) The method of claim 16, wherein the cholesterol-carrying liproprotein is LDL.
- 19. (Withdrawn) The method of claim 16, wherein the cholesterol-carrying liproprotein is VLDL.
- 20. (Withdrawn) The method of claim 16, wherein the second drug is selected from the group consisting of a statin, a bile acid sequestrant, nicotinic acid, probucol, a fibrate derivative, Neomycin, and cholestyramine.

21. (canceled)

U.S.S.N. 09/436,892 Amendment dated October 22, 2004 Reply to Office Action dated June 22, 2004

22-28. (canceled)

29. (Previously presented) The method of claim 9, wherein the control is low density lipoprotein in the absence of test compound.

30. (canceled)

- 31. (Previously presented) The method of claim 15, wherein the formation of the complex is determined by a sandwich immunoreactivity assay.
- 32. (Previously presented) The method of claim 15, wherein the formation of the complex is determined using agarose electrophoresis.

33-34. (Canceled)

- 35. (Previously presented) The method of claim 15, wherein the cholesterol-containing low-density lipoprotein is LDL.
- 36. (Previously presented) The method of claim 15, wherein the cholesterol-containing low-density lipoprotein is VLDL.
- 37. (Withdrawn) A method for assessing whether a compound enhances the uptake and clearance of a cholesterol-containing low density lipoprotein comprising:
- i) allowing the compound to form a complex with a labeled cholesterol-containing lipoprotein;
 - ii) isolating the complex;
 - iii) allowing the complex to incubate with a cell culture;
- iv) measuring the uptake of the labeled cholesterol containing lipoprotein into the cells.

- 38. (Withdrawn) The method of claim 37, wherein the cell culture is composed of hepatic cells.
- 39. (Withdrawn) The method of claim 37, wherein the uptake of labeled cholesterol containing lipoprotein is determined in the presence of an excess amount of unlabeled cholesterol-containing lipoprotein.
- 40. (Currently Amended) A method to determine if a compound causes a change in the structure of apolipoprotein B-100 in a cholesterol-containing low density lipoprotein thus increasing the binding of an epitope on the apolipoprotein B-100 to an LDL-receptor, comprising:
- (i) mixing the compound with and allowing it to bind to cholesterol-containing low density lipoprotein forming a complex;
- (ii) exposing the complex to a first capture antibody that is attached to a solid phase material and is directed to the epitope on apolipoprotein B-100 that binds to the LDL-receptor, forming a combination;
- (iii) adding to the combination a second antibody to which is attached a label <u>and</u> binds the combination;
- (iv) quantifying the amount of the captured complex by quantifying the amount of label; and
- (v) comparing the amount of cholesterol-containing low density lipoprotein quantified in step (iv) to a control, wherein an increase in the amount of cholesterol-containing low density lipoprotein captured indicates an increased binding to the low density lipoprotein receptor.
- 41. (Previously presented) The method of claim 40, wherein the control is low density lipoprotein in the absence of test compound.